REMARKS

Claims 1-31 are presented; claims 3, 4, 6, and 11 have been cancelled. Claims 14-25 are withdrawn. Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks. No new matter is presented and support for the amendments can be found in the original claims, and on pages 34-37 of the specification. Applicants appreciate the withdrawal of many of the grounds of rejection.

The Objection of Claim 6

In paragraph 7 of the Office Action, claim 6 was objected to by the Examiner for being grammatically incorrect. Claim 6 has been cancelled, obviating the objection.

The Rejection of Claims 1-2, 5-10, 12-13, and 26-27 under 35 U.S.C. §112, 1st Paragraph

Claims 1-2, 5-10, 12-13, and 26-27 were rejected under 35 U.S.C. §112, 1st paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner alleges that there an insufficient number of exemplified species of *Methylophilus* bacteria to adequately describe the genus.

Applicants respectfully disagree with the above assertions and allegations, and respectfully assert that claimed invention is fully and adequately described by the disclosure. Applicants, however, have amended the claims to the particular biosynthetic enzyme(s), and said enzyme's particular structure. With all the claims now limited to the particular dihydrodipicolinate synthase and/or aspartokinase, it is respectfully asserted that the genus is adequately described in that there is a respresentative number of species described to support the claim to the genus. Not every member of genus needs to be exemplified; some experimentation is allowed, as long as it is not undue. With 9 representative species supporting the small genus of the *Methylophilus methylotrophus* strain of bacteria, the necessary experimentation to determine other members of this genus is minimal and routine. In light of the amendments and the above comments, it is respectfully requested that the rejection be withdrawn.

Claims 1-1, 5-10, 12-13, and 26-27 were rejected under 35 USC 112, 1st paragraph because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully disagree with the above assertions and allegations, and respectfully assert that claimed invention is fully and adequately enabled by the teachings in the specification. Applicants, however, have amended the claims to the particular biosynthetic enzyme(s), and said enzyme's particular structure. With all the claims now limited to the particular dihydrodipicolinate synthase and/or aspartokinase, it is respectfully asserted that the full scope of the claims are clearly enabled so that a person ordinarily skilled in the art could make/and use the invention commensurate in scope with these claims.

The Examiner's arguments focus on the undue experimentation required to determine all *Methylophilus* bacteria having the desired characteristics. Now that the claims are limited to the particular biosynthetic enzymes, as defined by structure, the experimentation necessary to determine species other than the 9 exemplified in the specification that would fall within the scope of the claims is clearly not undue, but routine. Methods of transformation and expression of DNA into the particular strain are routine, as are the methods for measuring L-amino acid production. Furthermore, the genes and proteins which are altered are not novel sequences, but are known in the art. The prior art must be considered when determining undue experimentation and undue breadth of claims, and there is a body of literature of the genes/proteins, their sequences, and their activities in various strains of bacteria. One of ordinary skill, armed with the knowledge in the art of the claimed genes/proteins, the exemplified mutations of the genes and proteins, and the high level of skill in this art, would clearly be able to determine other species that when transformed into the particular claimed strain of *Methylophilus* would have the activity of producing L-amino acids.

In light of the amendments and the above comments, it is respectfully requested that the rejection be withdrawn.

The Rejection of Claims 1-2 under 35 U.S.C. §102

Claims 1-2 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Barth *et al.* as evidenced by Voet *et al.*. The Examiner states that Barth *et al.* teaches DHFR transformation of *M. methylotrophus* which resulted in higher activity of the expressed DHFR, and refers to an inherent production of L-amino acids. Claims 1 and 2 have been amended to recite that the biosynthetic enzyme activity is either dihydrodipicolinate synthase or aspartokinase, which does not encompass DHFR.

In light of the amendments and the above comments, it is respectfully requested that the rejection be withdrawn.

The Rejection of Claims 1-2, 5-9, 12-13, and 26-27 under 35 U.S.C. §103

Claims 1-9, 11-13, and 26-27 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Kojima et al in view of Barth *et al.*, DeMaeyer *et al*, and Kim *et al.*.

Applicants disagree with the maintainence of the above rejections and the Examiner's explanation of the rejection, and respectfully request reconsideration and withdrawal of the rejection for the following reasons. As described in the Introduction of Kim et al. (page 105), it had been difficult to introduce mutations in methylotrophs, including *Methylophilus methylotrophus*, by methods conventionally used for such commonly-used microorganisms as *E. coli*. This fact suggests that *Methylophilus methylotrophus* is differernt from *E. coli* and other microorganisms regarding various properties including plasma membrane structure, metabolic pathways, and regulatory mechanisms of the metabolic pathways. Differences such as these between methylotroph-type microorganism and *E.coli* were also suggested in the prior art (see argument to previous rejections, filed June 23, 2004). Therefore, there had been difficulty in modifying a methylotroph-type microorganism, as compared to commonly-used microorganisms such as *E.coli*. Since *Methylophilus methylotrophus* is also a methylotroph-type microorganism, it had also been difficult to modify, and therefore, a person skilled in the art would not expect to obtain a strain of *Methylophilus methylotrophus* having L-amino acid-producing ability by modifying it in the same or similar way as Kojima et al..

Barth et al. and DeMaeyer et al. fail to cure the deficiencies of Kojima et al.. These

references disclose respectively that DHFR or α1 interferon was successfully expressed in *Methylophilus methylotrophus*. These proteins, however, do not effect intracellular L-amino acid composition. Furthermore, it was expected that upon introduction of a gene(s) encoding L-amino acid biosynthetic enzyme(s), the *Methylophilus methylotrophus* might not grow well as a result of an imbalance in the intracellular L-amino acid composition caused by enhanced expression of these gene(s). One of ordinary skill in the art would be unable, therefore, to obtain a strain of *Methylophilus methylotrophus* which has an ability to produce L-amino acids based upon the teachings of Barth and DeMaeyer. In contrast, the instant invention was unexpected in light of the above teachings, and hence is unobvious over the combination of the cited prior art.

The teachings of Kim et al., either alone or in combination with the above teachings, also fail to make up for any deficiencies of Kojima. This reference fails to demonstrate that L-amino acids had actually been produced by a strain of *Methylophilus methylotrophus*. Furthermore, the reference only alludes to the potential commercial value of general methylotrophic bacteria, but fails to teach *Methylophilus methylotrophus*, and even suggests that "progress in this are has been slow" (see the introduction on page 105). Such a mere mention fails to provide sufficient motivation, and certainly does not provide a reasonable expectation of success to the skilled art worker when combining the teachings of the cited references.

For these reasons and in light of the amendments to the claims, Applicants respectfully assert that the claims are free of the prior art and respectfully request that the above rejections be withdrawn.

Claims 1-4, 7, and 12-13 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Wang et al. in view of Barth *et al.*, DeMaeyer *et al*, and Kim *et al.*.

Applicants disagree with the above rejections and the Examiner's explanation of the rejection, and respectfully request reconsideration and withdrawal of the rejection for the following reasons. The teachings of Wang et al. are similar to those of Kojima (using *E. coli* as a host), and the above arguments regarding the differences between methylotrophs and *E. coli* apply here as well. More specifically, the difficulties known in the art in modifying a methylotroph-type microorganism, as compared to commonly-used

microorganisms such as *E.coli*, negate any expectation of success for a person skilled in the art in being able to obtain a strain of *Methylophilus methylotrophus* having L-amino acid-producing ability by modifying it in the same or similar way as Wang et al.. Again, the teachings of Barth *et al.*, DeMaeyer *et al*, and Kim *et al.* fail to make up for the deficiencies of Wang et al. for the reasons stated above. More specifically, the mere mention of potential commerical value of general methylotrophic bacteria fails to provide sufficient motivation to combine the teachings, and certainly does not provide a reasonable expectation of success to the skilled art worker when combining the teachings of the cited references.

For these reasons and in light of the amendments to the claims, Applicants respectfully assert that the claims are free of the prior art and respectfully request that the above rejections be withdrawn.

CONCLUSION

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Steadman believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, he is invited to call on the number below.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the undersigned respectfully requests that she be contacted immediately.

Respectfully submitted,

By: _____

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